Nucleophilic Substitution in the Mechanistic Border-line Region

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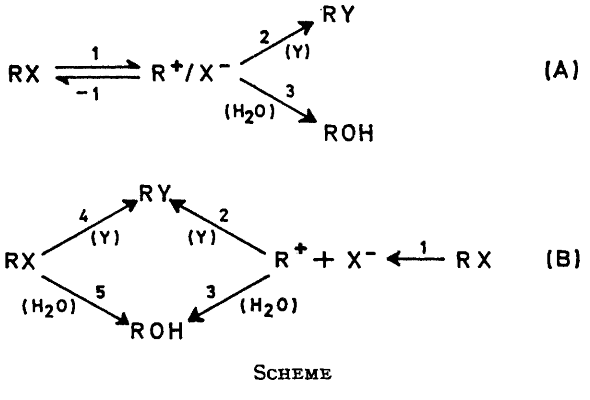
Summary It has been claimed that nucleophilic substitution in the mechanistic border-line region occurs by a single mechanism *via* an intermediate ion-pair, but it is now shown that the relevant results are equally consistent with concurrent unimolecular and bimolecular processes.

IT has recently been suggested[1] that all nucleophilic substitutions take place *via* an intermediate ion-pair (see Scheme A) and that direct bimolecular (S_N2) attack on the substrate occurs seldom, if ever. This conclusion was mainly based on the effect of added nucleophiles (Y) on the decomposition of organic chlorides and sulphonates (RX) in aqueous solvents[1a,2,3] for systems which would normally have been considered to react in the vicinity of the mechanistic border-line region which separates mechanisms S_N1 and S_N2. The results were considered consistent with (A) and not with concurrent S_N1 and S_N2 processes (Scheme B) but it is now shown that both (A) and (B) account equally well for the findings.

For the systems under consideration any RY formed is stable so that, neglecting any reaction between R^+ and X^-, the reaction schemes become:



SCHEME

Assuming (*cf.* ref. 1) that $[Y] \gg [RX]$

$$k = \frac{1}{t}\ln\frac{[ROH]_\infty - [ROH]_0}{[ROH]_\infty - [ROH]} = -\frac{1}{[RX]}\frac{d[RX]}{dt}$$

and $P = [RY]_\infty/[ROH]_\infty = d[RY]/d[ROH]$. Hence, for Scheme (A)

$$k = k_1^A \frac{1 + m[Y]}{1 + x + m[Y]},\ P = m[Y] \tag{1}$$

where $x = k_{-1}^A/k_3^A$ and $m = k_2^A/k_3^A$. For Scheme (B)

$$k = k_1^B + k_5^B + k_4^B\,[Y],\ P = [Y]\left\{\frac{\beta k_1^B + k_4^B\,(1 + \beta[Y])}{k_1^B + k_5^B\,(1 + \beta[Y])}\right\} \tag{2}$$

where $\beta = k_2^B/k_3^B$. Sneen and Larsen[1] excluded Scheme (B) on the qualitative grounds of an approximately linear variation of [Y] with P_{obs} but not with k_{obs} (see equations 1 and 2).

However, for reasonable values of the various disposable parameters, equations (1) and (2) lead to very similar standard deviations of the calculated product ratios (P) and rate coefficients (k) about the observed quantities, showing that no distinction between Schemes (A) and (B) is possible. This is illustrated in the Table for the hydrolysis of s-octyl methanesulphonate.[1a] Most of the assumptions made in the calculations (see Table, footnotes) are similar to those in the original work but a negative salt effect has now been postulated for the S_N2 reaction between an anion and RX, as generally accepted.[4] In addition, figures are reported for several values of k_5^B/k_1^B since it is not known whether the substrate undergoes entirely S_N1 hydrolysis ($k_5^B = 0$) in highly aqueous solvents, like the s-alkyl-toluene-*p*-sulphonates;[5] bimolecular reaction of RX with the strong nucleophile (Y) but not with the weakly nucleophilic water is, of course, perfectly feasible.[6]

Similarly, it can easily be shown that no distinction between Schemes (A) and (B) is allowed by the results for reaction in aqueous acetone of 4-methoxybenzyl chloride[2] (initial rates, $Y = N_3^-$) or benzoyl chloride[3] ($Y = o\text{-}NO_2C_6H_4NH_2$) where the bimolecular processes are retarded by Y; Scheme (B) was originally suggested for both systems.[2,3]

The hydrolysis of s-octyl methanesulphonate in the presence of azide ions

$\sigma_Q = [\Sigma(Q_{\text{calc}}-Q_{\text{obs}})^2/n]^{\frac{1}{2}}$; P_{calc} and k_{calc} from equations (1) and (2); $k_1^A, k_1^B, k_5^B = k^0(1 + b[N_3^-])$, $k_4 = k_4^0(1 - 0{\cdot}336[N_3^-])$

		25% aq. dioxan[a,b]			30% aq. dioxan[a,c]		
Scheme	k_5^B/k_1^B	$10^4\sigma_k$	σ_P	β	$10^4\sigma_k$	σ_P	β
(A)	—	0·063	0·130	—	0·178	0·139	—
(B)	0	0·064	0·107	2·29	0·165	0·151	2·51
	0·2	0·064	0·120[d]	3·00	0·165	0·149[d]	3·60
	0·5	0·064	0·141[d]	4·40	0·165	0·149[d]	5·50
	1·0	0·064	0·176[d]	7·40	0·165	0·185[d]	11·00

[a] k^0, b, m, and x from Sneen and Larson[1a].

[b] $10^4k_4^0 = 11{\cdot}32$, $n = 4$, $[N_3^-] = 0{\cdot}076$—$0{\cdot}237$M.

[c] $10^4k_4^0 = 9{\cdot}74$, $n = 7$, $[N_3^-] = 0{\cdot}054$—$0{\cdot}311$M.

[d] The salt effect has been assumed to be the same for k_1^B and k_5^B. Smaller values of σ_P can be obtained by making the very reasonable postulate that the ionisation process (k_1^B) is more sensitive to the presence of electrolytes than S_N2 hydrolysis (k_5^B).

The general implications of Scheme (A) will be discussed elsewhere but it must be stressed now that the requirement of no direct bimolecular (S_N2) attack on the substrate can lead to difficulties even in mechanistically border-line systems. For example, the activation parameters for the hydrolysis of 4-phenoxybenzyl chloride strongly suggest an entirely S_N1 process,[5] corresponding to $x \ll 1$ in Scheme (A).[1a] However, the more than ten-fold increase of the initial rate of decomposition in the presence of 0·03M-azide ions[6b] and the accompanying observation of good second-order kinetics up to 80% reaction (substrate initially at 0·02M) require $x > 100$. No similar inconsistency arises for reaction by Scheme (B).

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[2] G. Kohnstam, A. Queen, and B. Shillaker, *Proc. Chem. Soc.*, 1959, 157.

[3] V. Gold, J. Hilton, and E. G. Jefferson, *J. Chem. Soc.*, 1954, 2756.

[4] See for example: E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Rinehardt and Winston, New York, 1960 p. 257; R. A. Sneen and H. W. Robbins, *J. Amer. Chem. Soc.*, 1969, **91**, 3100; and references there cited.

[5] G. Kohnstam, *Adv. Phys. Org. Chem.*, 1967, **5**, 121; and references there cited.

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